

On page 28, line 9, change "(1978)" to --(1978)--.

On page 31, line 16, change "prepared," to --prepared and--.

On page 32, line 1, change "Examples" to --examples--; in line 4, change "low" to --lower--; in line 13, change "sites" to --site--.

On page 33, line 33, change "double stranded" to --double-stranded--.

On page 34, line 1, change "Id." to --supra--; in line 8, change "Id." to --supra--; in line 10, change "short length single or double stranded" to --short-length single- or double-stranded--; in line 29, change "cation exchange" to --cation-exchange--.

On page 44, line 24, delete "(Figure 1)".

On page 50, line 7, change "tPA" to --t-PA--.

On page 53, line 25, change "Site Directed" to --Site-Directed--.

On page 54, line 16, change "deoxyribonucleotides" to --deoxyribonucleotide triphosphates--; in line 17, after "deoxyriboadenosine" add --triphosphate--; after "deoxyriboguanosine" add --triphosphate--; in line 18, after "deoxyribothymidine" add --triphosphate--; in line 19, after "deoxyribocytosine" add "triphosphate" and change "(aS)" to --(aS)--; in line 20, change "deoxynucleotides" to --deoxynucleotide triphosphates--; in line 25, change "(aS)" to --(aS)--.

On page 55, line 17, change "over" to --through-- and change "Sephacryl" to --Sephacrose--.

On page 61, line 3, col. L of Table II, change "PLasma" to --Plasma--.

In the Claims:

In claim 11, line 1, replace "claim 10" with --claim 1--.

In claim 15, line 1, replace "claim 13" with --claim 1--.

In claim 19, line 1, replace "claim 13" with --claim 1--.

Please add the following new claims:

60. A fibrinolytically active tissue plasminogen activator (t-PA) amino acid sequence variant having an asparagine at amino acid position 103 of the native human t-PA, or having an asparagine at amino acid position 105 and a serine or threonine at amino acid position 107 of the native human t-PA, as part of the Asn-X-Ser or Asn-X-Thr tripeptidyl sequence, wherein X is any amino acid except proline.--

--61. The t-PA variant of claim 60 additionally having an amino acid substituted in the amino acid region 296-299 of the native human t-PA.--

¹⁶
--62. The t-PA variant of claim ~~61~~⁶⁰ having alanine substituted at each of amino acid positions 296-299 of the native human t-PA.--

¹⁸
--63. The t-PA variant of claim ~~61~~⁶⁰ which additionally has at least one amino acid selected from the group of amino acid positions 117-119, 184-186, 218-220, and 448-450 substituted with another amino acid such that glycosylation cannot occur at at least one of amino acid positions 117, 184, 218, or 448.--

¹⁷
--64. The t-PA variant of claim ~~62~~⁶⁰ which additionally has at least one amino acid selected from the group of amino acid positions 117-119, 184-186, 218-220, and 448-450 substituted with another amino acid such that glycosylation cannot occur at at least one of amino acid positions 117, 184, 218, or 448.--

¹⁹
--65. A fibrinolytically active human tissue plasminogen activator (t-PA) variant having an asparagine substituted at amino acid position 103 of the native human t-PA, as part of the Asn-X-Ser or Asn-X-Thr tripeptidyl sequence, wherein X is any amino acid except proline.--

--66. The t-PA variant of claim 65 additionally having an amino acid substituted in the amino acid region 296-299 of the native human t-PA.--

²⁰
--67. The t-PA variant of claim ~~66~~⁶⁵ having alanine substituted at each of amino acid positions 296-299 of the native human t-PA.--

²⁴
--68. The t-PA variant of claim ~~66~~⁶⁵ which additionally has at least one amino acid selected from the group of amino acid positions 117-119, 184-186, 218-220, and 448-450 substituted with another amino acid such that glycosylation cannot occur at at least one of amino acid positions 117, 184, 218, or 448.--

²¹
--69. The t-PA variant of claim ~~67~~⁶⁶ which additionally has at least one amino acid selected from the group of amino acid positions 117-119, 184-186, 218-220, and 448-450 substituted with

another amino acid such that glycosylation cannot occur at at least one of amino acid positions 117, 184, 218, or 448.--

--70. A composition for treating a vascular disease or condition comprising a therapeutically effective amount of t-PA variant of claim 68.--

--71. A composition for treating a vascular disease or condition comprising a therapeutically effective amount of t-PA variant of claim 69.--

--72. A method of treating a vascular disease or condition in a patient comprising administering the composition of claim 70.--

--73. A method of treating a vascular disease or condition in a patient comprising administering the composition of claim 71.--

Respectfully submitted,
GENENTECH, INC.

Ginger R. Dreger
Registration No. 33,055

Dated: 22 March 1993
460 Point San Bruno Blvd.
So. San Francisco, CA 94080-4990
(415) 225-3216